REMARKS/ARGUMENTS

Upon entry of this amendment, claims 1, 3 and 6-8 will be amended, whereby claims 1-8 will remain pending.

By the amendment herein, claims 1, 3 and 6 have been amended to include language as suggested by the Examiner so that "may comprise" has been changed to "are optionally substituted with". Moreover, claims 6-8 have been amended to even more clearly be directed to compositions.

Reconsideration and allowance of the application are respectfully requested.

Consideration Of Information Disclosure Statements

Applicants express appreciation for the inclusion with the Office Action of signed copies of Forms PTO-1449, whereby the Examiner's consideration of the Information Disclosure Statement, filed February 2, 2007, is of record.

Applicants are submitting on even date herewith a Supplemental Information Disclosure Statement. The Examiner is requested to consider the information cited therein, and to forward an initialed copy of the Form PTO-1449 submitted therewith with the next communication from the Patent and Trademark Office.

Claim Of Priority

Applicants also express appreciation for the acknowledgement of the claim of foreign priority as well as receipt of the certified copy of the priority application in this national stage application.

The Office Action improperly contends that foreign priority has not been granted because an English-translated version of the foreign priority document has not been filed. Applicants

submit that this contention is not correct as an English translation is not required to establish a claim of priority. An English translation is only needed if it is desired to overcome intervening prior art. Accordingly, the Examiner is requested to clarify this erroneous indication in the next communication from the Patent and Trademark Office.

Formal Drawings

Applicants express appreciation for the indication that the drawings filed with the application have been accepted.

Claim Objections

The objections indicate that in claim 1, line 5, "may comprise" should be ---are optionally substituted with---, and that claims 6-8 should use composition language.

In response, claims 1, 3 and 6 have been amended to include the "are optionally substituted with" language preferred by the Examiner. Moreover claims 6-8 have been amended to even more explicitly recite composition language.

According, the objections should be withdrawn.

Response To Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as it is asserted that while the specification is enabling for using compounds of formula (I) for treating cells *in vitro*, it does not reasonably provide enablement for using compounds of the formula (I) for treating cancer, *in vivo*. The rejection appears to be essentially contending that there is no established correlation

between *in vitro* activity and accomplishing treatment of "treating cancer", *in vivo*, despite the guidance provided in the specification.

In response to this ground of rejection, Applicants submit that the subject matter recited in claims 7 and 8 is enabled so that one having ordinary skill in the art would be capable of practicing the claimed subject matter without undue experimentation, especially in view of the knowledge of one having ordinary skill in the art and the guidance provided in the originally filed application. Thus, Applicants respectfully submit that the rejection is without appropriate basis, and does not set forth a *prima facie* case of a lack of enablement, whereby the rejection should be withdrawn.

As disclosed in Applicants' originally filed specification, at pages 2 to 5, the level of skill in this art is high, and there is a correlation of similar compounds to the treatment of cancer.

Further, as the rejection realizes, experiments are provided in Applicants ' specification. For example, the Examiner's attention is directed to pages 24 and 25, and Fig. 1.

Regarding *in vitro* experimentation, the Examiner is reminded that *in vitro* experimentation is permissible, and the initial burden is on the examiner to give reasons for the lack of enablement. The Examiner must establish, with sufficient reasons, a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. In the instant situation, the rejection merely makes the assertion that there is no established correlation between *in vitro* activity and "treating cancer", *in vivo*, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use the instant compounds since there is no description of an actual method wherein "treating cancer" in a host is treated.

In contrast to these assertions, Applicants note that there is no requirement for working examples. However, in the instant situation, Applicants have provided working examples which

are sufficiently correlated to the claimed subject matter. The rejection has not shown any scientific evidence to refute Applicants' showing, and has not made a utility rejection asserting that the claimed subject matter lacks utility.

Still further, Applicants submitting with a Supplemental Information Disclosure Statement on even date herewith a copy of Uchiyama et al., Biochimica et Biophysica Act, 1771 (2007) 103-112. A review of Figs. 4 to 9 of Uchiyama et al. on pages 108-110 shows biological activity of a compound accordingly to the present invention, i.e., 2ccPA. Especially, Fig. 9 shows the effect of 2ccPA on the number of lung tumor modules as *in vivo* data.

Thus, Applicants submit that the nature of the invention, the level of skill and predictability in the art, Applicants' guidance including examples, the claim scope, and a lack of undue experimentation are sufficient so that a *prima facie* rejection has not been established.

For at least the reasons provided herein, Applicants submit that the claims are enabled, whereby this ground of rejection should be withdrawn.

Response to Indication of Allowable Subject Matter

Applicants express appreciation for the allowance of claim 5, but for the reasons set forth below submit that each of the pending claims is patentable over the prior art of record.

Response To Art Based Rejections

The following rejections are set forth in the Office Action.

(a) Claims 1, 2 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by (1) Kawai et al., publication, Synthesis and Physiological Effects of Cyclic Lysophosphatidic Acid and Carba-Derivative, "The 23rd Symposium on Progression Organic Reactions in Life Science,

"November 17 and 18, 1997, The Pharmaceutical Society of Japan, pp. 1-9; or (2) Liliom et al., CAS: 125:265929.

(b) Claims 1, 2, 4 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mukai et al., US 2004/0214799.

(c) Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al., publication, Synthesis and Physiological Effects of Cyclic Lysophosphatidic Acid and Carba-Derivative, "The 23rd Symposium on Progression Organic Reactions in Life Science, "November 17 and 18, 1997, The Pharmaceutical Society of Japan, pp. 1-9.

(d) Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mukai et al., US 2004/0214799.

In response to these grounds of rejection, Applicants initially point out that the rejections fail to address that Mukai et al. (as disclosed in Applicants' specification in the last paragraph on page 5 as family member JP 2001-150685), is structurally different from Applicants' recited compound. In particular, in the compound of Mukai et al., as well as Kawai et al., $-CH_2$ is present on the Sn-3 position of glycerol structure. In contrast, in Applicants' claimed compound, the $-CH_2$ is present on the Sn-2 position of glycerol structure. Therefore, the compounds disclosed by Mukai et al. and Kawai et al. are different from the compounds recited by Applicants.

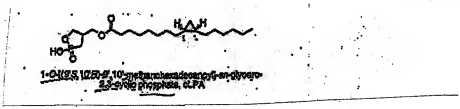
Accordingly, for at least this difference, which difference is not addressed in the rejections of record, the anticipation and obviousness rejections based upon Mukai et al. and Kawai et al. should be withdrawn.

Additionally, so that the record is complete, Mukai et al. should not be considered to qualify as prior art under 35 U.S.C. 102 because Mukai et al. published on October 28, 2004, which is after Applicants' June 10, 2003 International filing date, and does not constitute 102(e) prior art because

it published in Japanese. However, Applicants note the counterpart PCT application of Mukai et al. published as WO 02/094286 (cited in Applicants' Information Disclosure Statement), on November 28, 2002, and therefore would appear to constitute intervening art.

Regarding Liliom, the source document for Liliom is Molecular Biology, 1996, 50(3), 616-623 (hereinafter referred to as the "Liliom article"), and a copy of this document is submitted with the Supplemental Information Disclosure Statement filed on even date herewith.

A review of Fig. 1 on page 617 of the Liliom article shows the following chemical structure which is similar to the compound recited in Applicants' claims.



However, this chemical structure set forth in the Liliom article contains a clear error, and the compound recited in Applicants' claims is not anticipated by Liliom. Namely, the compound of Liliom is named as "1-0-{(9'S,10'R)-9',10'-methanohexadecanoyl}-sn-glycero-2,3-cyclic **phosphate**, cLPA" (Emphasis added). As one having ordinary skill in the art would readily understand, the term **"phosphate"** means compounds wherein 4 oxygen (O) atoms are bound to a phosphorus (P) atom. See, for example, Phosphate – Wikipedia, the free encyclopedia, 4 pages, downloaded from http://en.wikipedia.org/wiki/Phosphates, on January 13, 2009, and included in the Supplemental Information Disclosure Statement being filed on even date herewith. Therefore, one having ordinary skill in the art would readily understand from a review of Liliom that the name of the compound is not consistent with the illustrated chemical structure. In particular, $-CH_2-$ is

bound to the phosphorus atom in the chemical structure but this $-CH_2-$ is a clear error and should be –O- in accordance with the chemical name.

As further evidence which supports the fact that the chemical structure of Liliom contains an error, submitted with the Supplemental Information Disclosure Statement is a copy of Kobayashi et al., Tetrahedron Letters, Vol. 34, No. 25, 4047-4050, 1993, which is cited at page 617, left column, line 3 from the bottom of the Liliom article as Reference No. 25. The cLPA which is described in Kobayashi et al. is a natural compound (PHYLPA) which is indicated, at page 4049, last three lines, to be determined to be 16(sodium 1-0-[(9'S,10'R)-9',10'-methanohexadecanoyl}-sn-glycero-2,3-cyclic phosphate), wherein 4 oxygen (O) atoms are illustrated as bound to a phosphorus (P) atom. Kobayashi et al. nether teaches nor suggests any synthesis of the 2-carba cyclic phosphatidic acid derivative as claimed by Applicants. It is not possible to synthesize the 2-carba cyclic phosphatidic acid derivative of the present invention based upon the disclosure of Liliom and/or Kobayashi et al.

Since the listing of 1-0-{(9'S,10'R)-9',10'-methanohexadecanoyl}-sn-glycero-2,3-cyclic phosphate, cLPA in Liliom is an error that is obvious to one of ordinary skill in the art, it cannot be said to describe or suggest that compound to those in the art, and the public is not put in possession of the compound. See *In re Yale*, 168 USPQ 46, 48 (CCPA 1970).

Accordingly, for at least the reasons set forth above, the rejections of record should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the objections and rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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